U.S. Serial No. 09/812,633

Clean Version of Replacement Paragraphs and Claims Pending After Entry of Amendment

Please replace the paragraph starting on line 28 of page 3 with the following paragraph.

A further aspect of the invention encompasses a knockout mouse featuring a knockout mutation in a genomic mouse *Sal2* (*mSal2*) gene. This knockout mouse may also contain, for example, a nucleic acid construct including a mutant *Sal2* gene and this mutant Sal2 gene may be conditionally expressed. In a preferred embodiment, the mutant *Sal2* gene, for example a human *Sal2* gene, encodes a protein that contains a substitution of a Cys for the Ser at position 73 of SEQ ID NO.:1. However, the Sal2 protein may also be wild-type.

Please replace the paragraph starting on line 27 of page 34 with the following paragraph.

The *hSal2* gene has been mapped to chromosome 14q12 but was not recognized initially as a tumor suppressor gene. It was subsequently shown by others that this region of 14q is associated with a loss of homozygosity in 49% of ovarian cancers (Bandera et al., *supra*) and about 25 % of bladder cancers (Chang et al., *supra*). These findings, along with the underlying rationale of 'tumor host range' selection, suggest the possibility that *sal2* may function as a tumor suppressor. To test this possibility more directly, a screen for $p150^{sal2}$ expression was carried out on extracts of ovarian carcinomas (Fig. 7). Fig. 7 shows a Western blot of human ovarian tumors. The expression level of $p150^{sal2}$ in 20 ovarian carcinomas was compared with that of normal ovarian epithelial cells (N). Fifty micrograms of protein were loaded in each lane and blotted with polyclonal antibody against $p150^{sal2}$. Each ovarian carcinoma was labeled by its case number. Arrows indicate the normal position of p150. A polyclonal anti-p150 antibody made against the mouse protein clearly recognizes the human protein (Fig. 3B above). A band of the same apparent

molecular weight is seen in extracts of normal human ovarian epithelial cells ('HOSE').

1. (Amended) A method of identifying a mammal having or at risk of acquiring a proliferative disease, said method comprising at least one of the following steps:

(a) measuring the Sal2 protein level in a cell of said mammal relative to the Sal2 protein level in a mammal not having or being at risk for said proliferative disease;

(b) determining the presence or absence of an altered Sal2 protein in said mammal relative to a Sal2 protein in a mammal not having or being at risk for a said proliferative disease; or

(c) determining the presence or absence of a proliferative disease-associated alteration in a *Sal2* nucleic acid in said mammal relative to the nucleic acid sequence of SEQ ID NO.: 2 and SEQ ID NO.:4, wherein a decrease in said SAL2 protein level in step (a) or the presence of an alteration in steps (b) or (c) identifies a mammal as having or being at risk of acquiring a proliferative disease.

2. The method of claim 1, wherein said method is for identifying a mammal having a proliferative disease.

3. The method of claim 1, wherein said method is for identifying a mammal at increased risk of acquiring a proliferative disease.

4. The method of claim 1, wherein said mammal is a human.

5. The method of claim 4, wherein said proliferative disease-associated alteration comprises the substitution of a Cys for the Ser at position 73 of SEQ ID NO:1.

6. The method of claim 1, wherein said determining is done by polymerase chain reaction (PCR) amplification, single nucleotide polymorphism (SNP) determination, restriction fragment length polymorphism (RFLP) analysis, hybridization analysis, or mismatch detection analysis.

7. The method of claim 1, wherein said step (c) comprises the steps of:

(i) contacting a first nucleic acid probe which is specific for binding to a human *Sal2* nucleic acid containing a proliferation disease-associated alteration with a nucleic acid from a cell from said mammal under conditions which allow said first nucleic acid probe to anneal to complementary sequences in said cell; and

(ii) detecting duplex formation between said first nucleic acid probe and said complementary sequences.

8. The method of claim 7, wherein said first nucleic acid probe is derived from the human *Sal2* nucleic acid containing a proliferative disease-associated alteration.

9. The method of claim 7, further comprising a second nucleic acid probe, wherein said first and second nucleic acid probes are PCR primers, and wherein said human *Sal2* nucleic acid or a fragment thereof is amplified using PCR between steps (i) and (ii).

10. The method of claim 7, wherein said cell is from a physiological sample containing abnormally proliferating tissue.

11. The method of claim 7, wherein said cell is from a physiological sample of normal tissue.

12. The method of claim 7, wherein said alteration comprises the substitution of a Cys for the Ser at position 73 of SEQ ID NO:1.